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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,627	04/17/2001	Robert A. Scott	6514-11-BHJ	7296

29668 7590 03/26/2002

PFIZER, INC.
201 TABOR ROAD
MORRIS PLAINS, NJ 07950

EXAMINER
DI NOLA BARON, LILIANA

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/836,627	Applicant(s) COLE ET AL.	
	Examiner Liliana Di Nola-Baron	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25 and 28-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 28-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Applicant's amendment, filed on February 19, 2002, is acknowledged.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 21, 24, 25 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention refers to a drug delivery system comprising a HPMC capsule, in which the body and the cap are separately coated or two equal empty HPMC capsule halves are filled with a caplet and separately coated. Additionally, the invention refers to HPMC capsules having a sealing on the gap between the body and the cap. This is in contrast with the written description of the invention, where an overlapping region of capsule body and cap is mentioned (See p.3, line 20). The written description of the coating process claimed in the invention is insufficiently reproducible. The specification lacks direction and guidance regarding the claimed coating process and specific embodiments and illustrative examples pertinent to the scope of the invention. Due to the lack of guidance presented in the specification regarding the methodology of the claimed invention and the absence of working examples directed to a method of separately coating the different components of the HPMC capsule, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention.

3. Claims 1-25 and 28-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment to claims 1-25 and 28-31, changing the coating to a single aqueous coating, represents a departure from the specification and the claims as originally filed. The support pointed out by the Applicant, on page 4, line 9 to page 5, line 17 of the specification, provides the general teaching for a coating and does not provide support for a single aqueous coating.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 21, 22, 25 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Regarding claims 21, 22, 25 and 28, the application of separate coatings is inconsistent with a single aqueous coating, which is claimed in generic claim 1, thus rendering the claims indefinite. Additionally, claims 21, 22, 25 and 28 refer to a drug delivery system according to claim 1, but claim 1 reads on a drug delivery composition.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-25 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hatano et al., in view of Watts and further in view of Tanida et al. and Paulos.

The claimed invention refers to a drug delivery composition comprising a HPMC capsule provided with a coating for delivering a drug in the small intestine or colon.

Hatano et al. discloses a coated capsule containing an acidic substance, a polymer film and an enteric coating, for medicament delivery to any site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract (See e.g., p.3, lines 7-10). Hatano et al. explains that the enteric coating film protects the pharmaceutical preparation in the stomach and dissolves in the upper part of the small intestine, allowing the digestive juices to gradually penetrate and dissolve the acidic substance in the hard capsule. The acidic solution thus formed dissolves the capsule and the medicaments are released (See e.g., p.3, lines 11-19). Hatano et al. teaches that the pharmaceutical agents in the capsule can be selectively released at any desired site between the jejunum and the rectum and that any type of capsule can be used in the invention, including HPMC capsules (See e.g., p. 4, lines 6-20). Hatano et al. teaches that the

enteric polymer used for the enteric coating film must be soluble in a pH higher than 5 and includes a cellulose derivative, an acrylic polymer, a maleic copolymer, a polyvinyl derivative, shellac and the like (See e.g., p. 4, lines 46-49). Among the exemplary polymers, Hatano et al. includes HPMCP, methyl acrylate-acrylic acid copolymer, methyl acrylate-methacrylic acid copolymer and PVAP (See e.g. p. 4, lines 50-58 and p. 5, lines 1-9). Cellulose ester, which is mentioned in claim 15 of the present application as a component of the coating, is considered by the examiner for the purpose of the invention as a cellulose derivatives. Hatano et al. teaches that the amount of the enteric coating film is from 10 to 400% by weight based on the weight of the hard capsule (See e.g., p. 5, lines 41-46), and that the medicament in the capsule is not limited as long as it is orally administrable (See e.g., p. 8, lines 3-9). Hatano et al. teaches that preferable solvents for the coating solution are water and alcohol (See e.g., p. 9, lines 8-19). Additionally, Hatano et al. teaches that a sealing means can be provided around a joint of a body and a cap of the hard capsule and explains that the sealing agent can be any substance able to make the capsule's surface smooth at the joint, such as a water-soluble or insoluble polymer, a low pH-soluble or enteric polymer, a saccharide or the like (See e.g., p. 9, lines 23-55).
Thus, Hatano et al. provides a HPMC capsule provided with a coating for delivering a drug in the small intestine or colon. Hatano et al. is deficient in not including a redox sensitive material in the coating of the HPMC capsule.

Watts discloses a drug delivery composition for delivering a drug to the colonic region, comprising a coated starch capsule containing the drug (See e.g., p.3, lines 25-29). Watts teaches that the coating may be pH-sensitive, redox-sensitive or sensitive to particular enzymes or

bacteria, so that the capsules do not release the drug until it is in the colon (See e.g., p. 5, lines 9-14). Watts teaches that preferred coating materials are those which dissolve at a pH of 5 or above, including CAT, HPMCP, PVAP, shellac and cellulose esters, and that especially preferred materials are methylmethacrylates or copolymers of methacrylic acid and methylmethacrylate (See e.g., p. 5, lines 20-30 and p. 6, lines 1-22). Watts explains that, because of the high presence of microbial anaerobic organisms providing reducing conditions in the colonic region, the coating may comprise a redox-sensitive material, such as azopolymers, which are broken down enzymatically, or disulphide polymers (See e.g., p. 6, lines 24-30 and p. 7, lines 1-2).

Tanida et al. discloses a double-coated capsule having a HPMC base, for the release of drugs in the lower gastrointestinal tracts, specifically in the colon (See e.g., p.3, lines 18-52). Tanida et al. teaches that examples of the anionic copolymer, which constitutes the outer layer, include a copolymer of methacrylic acid with methyl methacrylate and HPMCP (See e.g., p. 3, lines 26-30). Tanida et al. teaches that the amount of the coating may vary depending upon the size of the capsule and is within a range of 0.08-0.13 mg/mm^2 (See e.g., p. 4, lines 22-28 and p. 18, claim 6).

Paulos discloses a method for making and administering a blinded oral dosage form (See e.g., col. 1, lines 7-11), and more specifically, a capsule containing a tableted medication and having an interlocking body portion and cap portion (See e.g., col. 5, lines 58-61). Paulos teaches that tablets of various sizes and shapes may be placed within the cap or body portion of the capsule

(See e.g., col. 8, lines7-18) and that the body and cap portions may be made of enteric materials (See e.g., col. 13, lines 3-19). Additionally, Paulos teaches that the capsules may be coated by a standard tablet coating process (See e.g., col. 13, lines 39-44) and that the method of the invention may include applying one or more coatings on the capsule, either before or after the tablet is placed within the capsule (See e.g., col.14, lines 26-37).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the drug delivery system disclosed by Hatano et al., by including a redox sensitive material in the coating of the HPMC capsule, as taught by Watts, and applying the suitable coating in the range recommended by Tanida et al., before or after filling the capsule with the caplet, as taught by Paulos. One of ordinary skill in the art would have been motivated to make such a modification to ensure a complete disintegration of the coating in the small intestine or the colon and prevent drug leaking in the stomach. Because of the teachings of Hatano et al., that any kind of medicament can be delivered to any desired site between the upper part of the small intestine and the lower part of the large intestine in the digestive tract, by controlling the amount and the kind of polymers used for the coating of the HPMC capsule, one of ordinary skill in the art would have a reasonable expectation that the HPMC capsule device of the present application would successfully deliver drugs to the small intestine or colon. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

9. Applicant's arguments filed on February 19, 2002 have been fully considered but they are not persuasive.

10. Applicant argues that there is support for claims 21, 24, 25 and 31 in the specification. It is noted that the support pointed out by Applicant reads on sealing the HPMC capsules after filling in the overlapping region of capsule body and cap. The disclosure is in contrast with the claimed invention, which reads on separately coating the body and the cap or two capsule halves, or on HPMC capsules having a sealing on the gap between the body and the cap.

11. In response to Applicant's argument, that the claimed invention is directed to a drug delivery composition having a single aqueous coating, it is noted that the support pointed out by the Applicant, on page 4, line 9 to page 5, line 17 of the specification, provides the general teaching for a coating and does not provide support for a single aqueous coating. Furthermore, the claimed invention reads on the application of separate coatings, which is inconsistent with a single aqueous coating,

12. In response to Applicant's argument, that Hatano et al. provides a drug delivery composition having multiple coatings, it is noted that the claimed invention reads on the application of separate coatings, thus requiring multiple coatings.

13. In response to Applicant's argument, that Hatano et al. discloses non-aqueous based coatings, it is noted that Hatano et al. contemplates both aqueous and non-aqueous coatings and teaches that water and alcohol are preferred solvents (See e.g., p. 9, lines 6-19).

14. In response to Applicant's argument, that Tanida discloses capsules having double coating, it is noted that the claimed invention reads on the application of separate coatings, thus requiring multiple coatings.

15. In response to Applicant's argument, that Watts discloses non-aqueous based coatings, it is noted that Watts contemplates both aqueous and non-aqueous coatings.

Conclusion

16. Claims 1-25 and 28-31 stand rejected.

17. Applicant's amendment has overcome the 35 U.S.C. 112, second paragraph, rejection of claim 10 of the previous Office action. Accordingly, that rejection is withdrawn.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.

March 20, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600